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Supporting Information

Photoenhanced Oxidative DNA cleavage with Non-Heme Iron(II) Complexes

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Experimental set-up of DNA cleavage

Reactions were carried out in 1.5 mL eppendorfs with open caps thermostatted at 37 °C in the dark. Light beams covered the whole area of top surface of reaction solutions and passed through the reaction solutions vertically. Figure S1 shows the set-up.

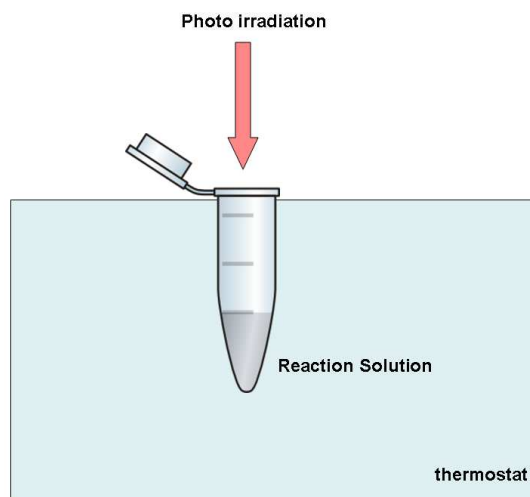


Figure S1: Experimental set-up for DNA cleavage experiments

Determination of irradiation power

The iron(III) oxalate/phenanthroline actinometer system was used to determine the light flux (R) of irradiation.¹ One example is shown in Figure S2.

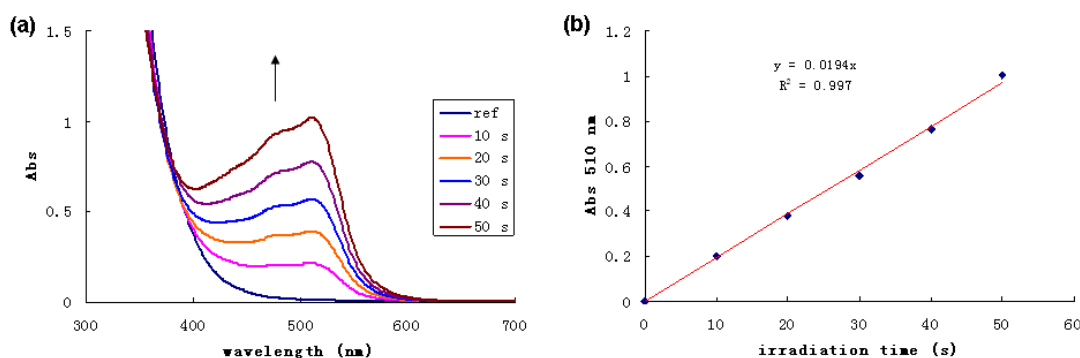


Figure S2: For CW laser 355 nm (3 mW), (a) absorption spectra of iron(III) oxalate (different irradiation time)/phenanthroline aqueous solutions; (b) absorption of iron(III) oxalate (different irradiation time)/phenanthroline aqueous solutions at 510 nm.

The power (P) at the sample was calculated using Equation (S1), in which E_p is the energy of one photon, h is Planks constant (6.626×10^{-34} Js), c is the speed of light (3.0×10^8 ms⁻¹), λ is the wavelength of light source (355, 400.8 and 473 nm, respectively). Table S1 shows the light flux (R) and power (P) at sample under different irradiation conditions.

$$P = E_p R = \frac{\hbar c}{\lambda} R \quad (S1)$$

Table S1: Light flux (R) and power (P) of different light sources at sample.

	Pulsed Laser		CW laser				
	355 nm		355 nm		400.8 nm	473 nm	
R (photons.s ⁻¹)	5.7×10^{15}	4.4×10^{16}	5.2×10^{15}	4.7×10^{15}	3.5×10^{16}	2.3×10^{15}	7.2×10^{16}
P (mW)	3.2	24.6	2.9	2.6	17.4	1.2	30.3

UV-Vis absorption spectra of Fe(II).L

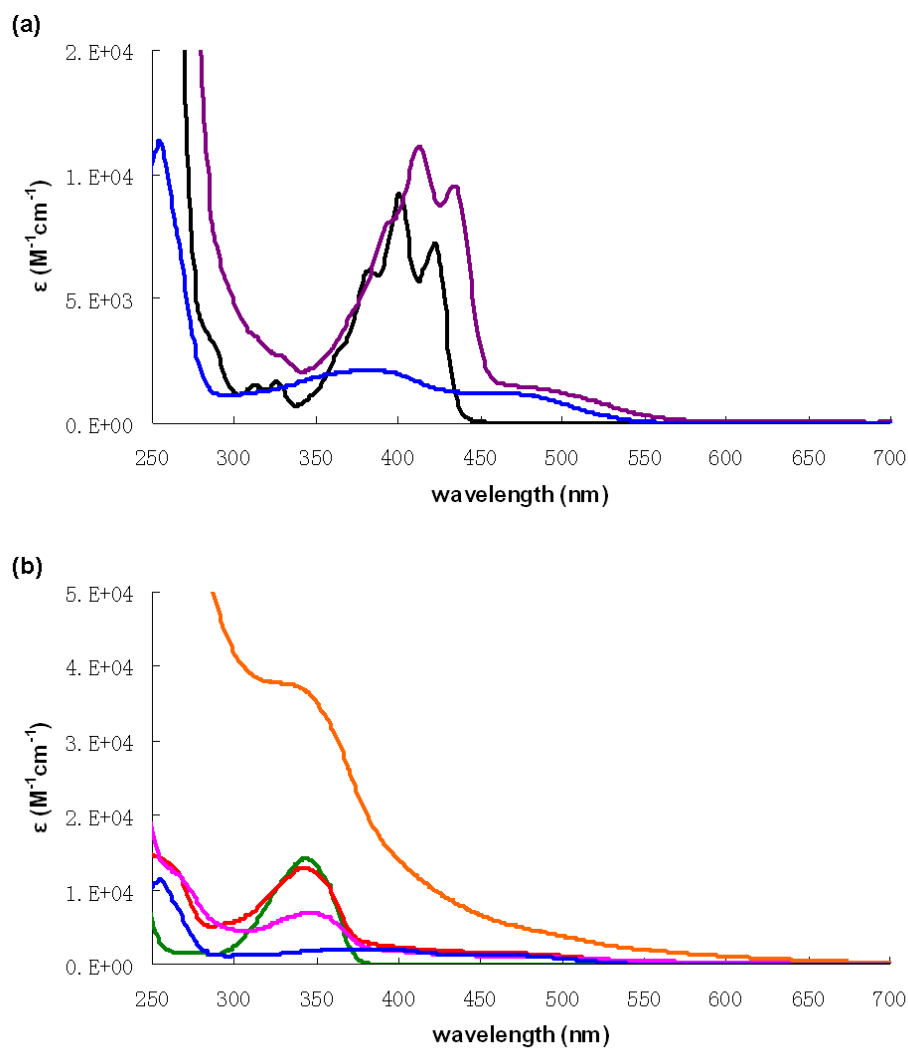


Figure S3: Normalized absorption spectra of (a) 9-aminoacridine (—), Fe(II)-1 (—) and Fe(II)-2 (—); (b) Fe(II)-1 (—), 1,8-naphthalimide (—), Fe(II)-3 (—), Fe(II)-4 (—) and Fe(II)-5 (—).

DNA cleavage under photo irradiation

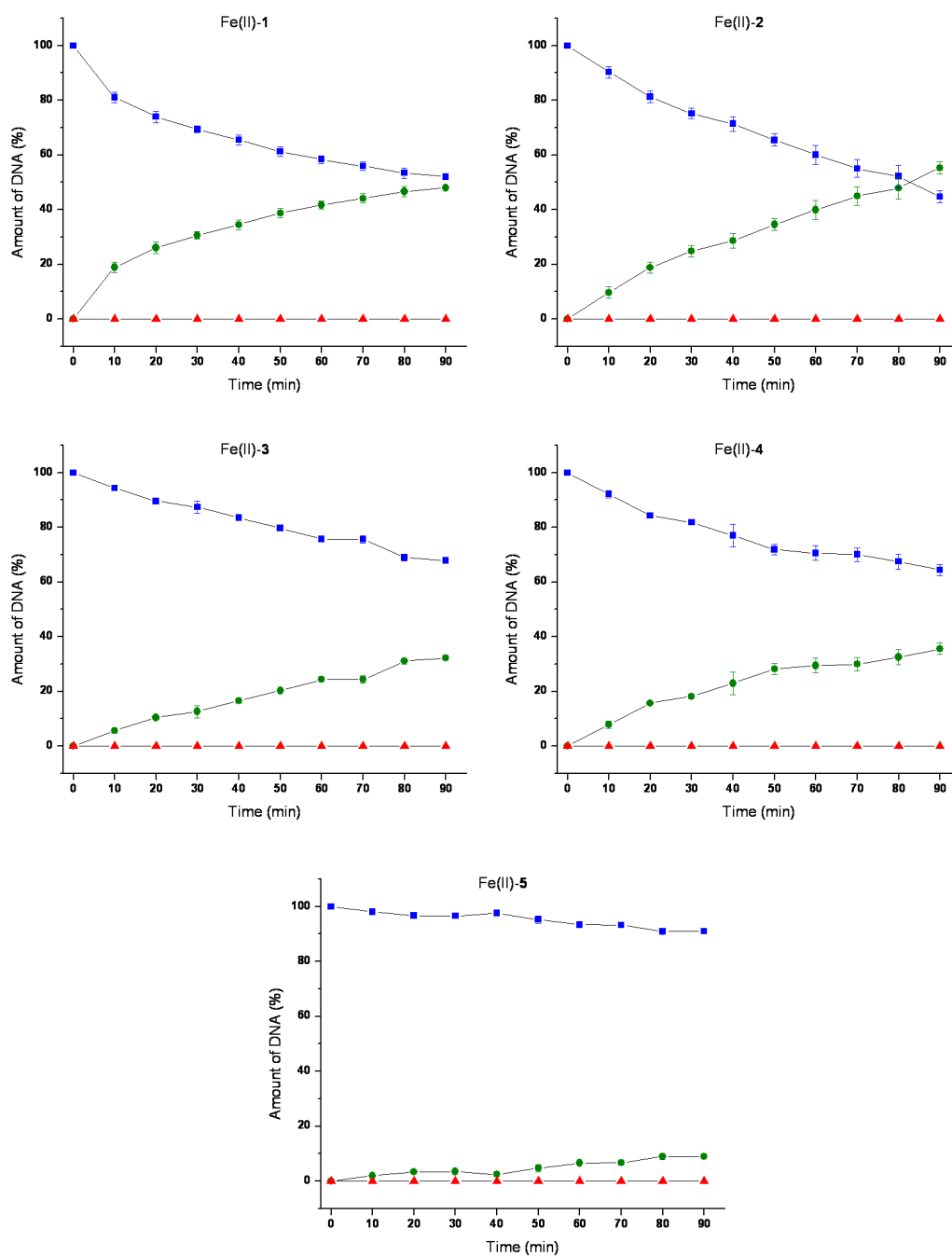


Figure S4: Time profile for cleavage of supercoiled DNA (■) to nicked (●) and linear (▲) DNA in 10 mM Tris-HCl (pH 8.0) at 37 °C with Fe(II) complexes of ligands **1-5** under photo irradiation at 473 nm (30.3 mW). Conditions: 1.0 μ M complex, 0.1 μ g/ μ l pUC18 plasmid DNA (150 μ M bp).

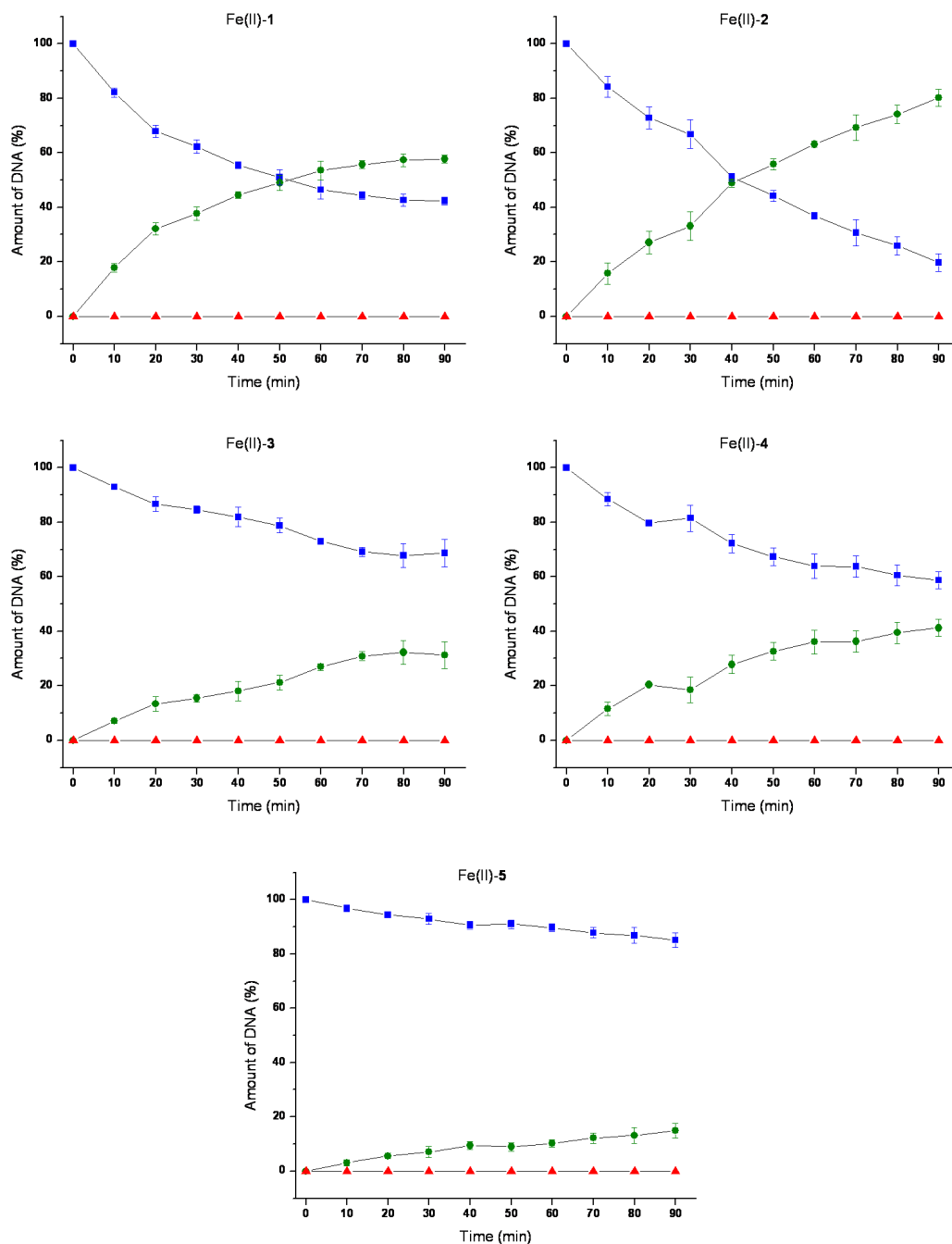


Figure S5: Time profile for cleavage of supercoiled DNA (■) to nicked (●) and linear (▲) DNA in 10 mM Tris-HCl (pH 8.0) at 37 °C with Fe(II) complexes of ligands **1-5** under photo irradiation at 400.8 nm (17.4 mW). Conditions: 1.0 μ M complex, 0.1 μ g/ μ l pUC18 plasmid DNA (150 μ M bp).

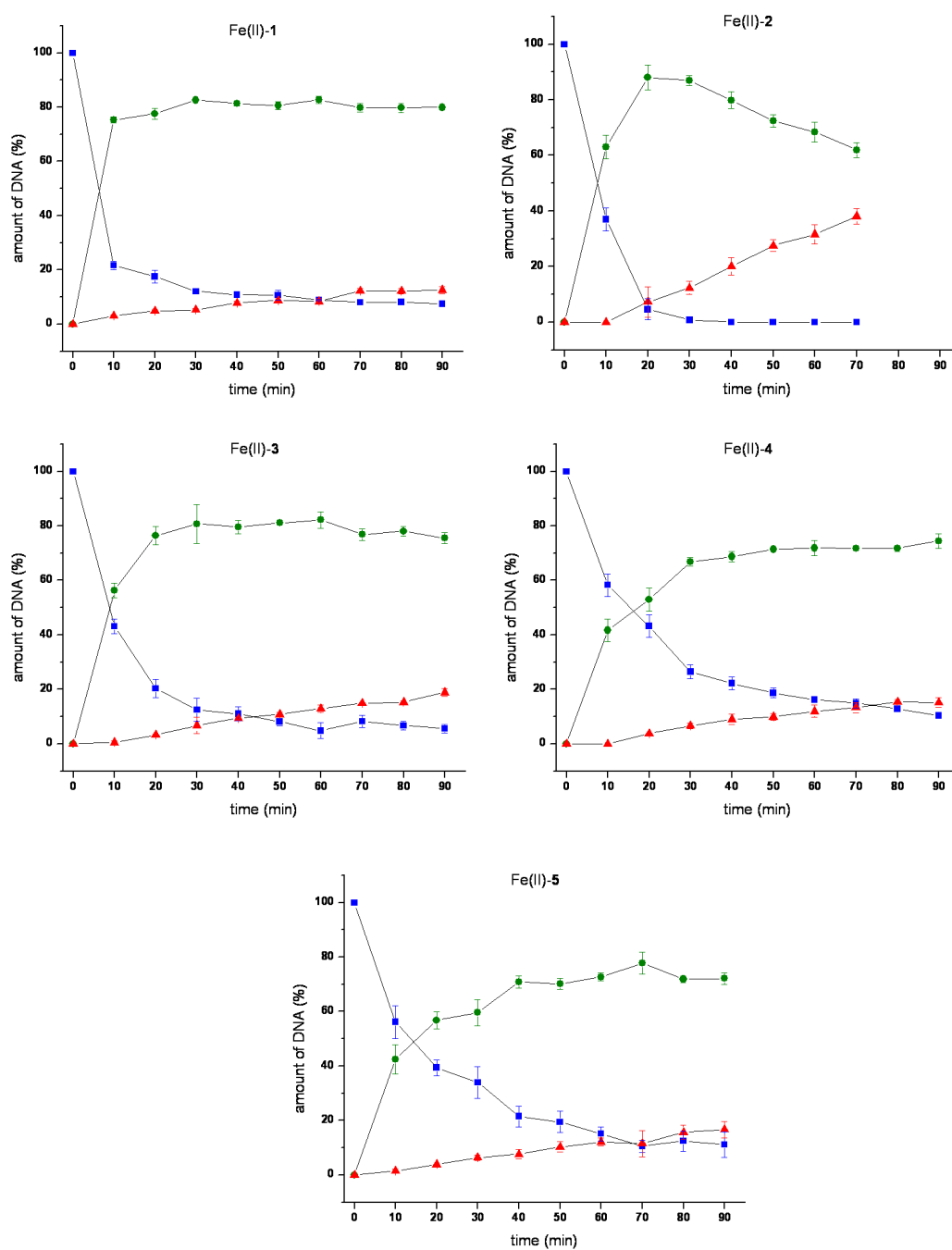


Figure S6: Time profile for cleavage of supercoiled DNA (■) to nicked (●) and linear (▲) DNA in 10 mM Tris-HCl (pH 8.0) at 37 °C with Fe(II) complexes of ligands **1-5** under photo irradiation at 355 nm (24.6 mW). Conditions: 1.0 μ M complex, 0.1 μ g/ μ l pUC18 plasmid DNA (150 μ M bp).

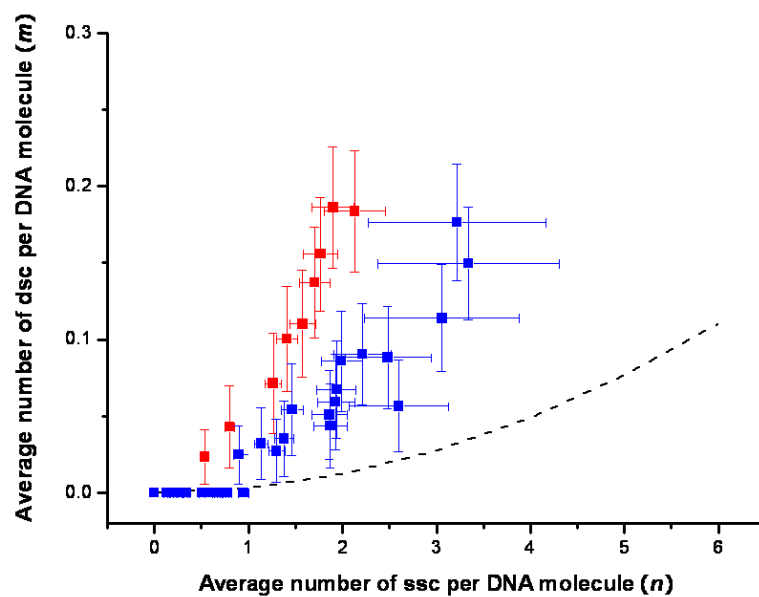


Figure S7: Number of double-strand cuts (m) as a function of single-strand cuts (n) per DNA molecule for Fe(II)-**4** in the presence of 1000 equiv. DTT (■) and under pulsed irradiation at 355 nm (24.6 mW) (■). Error bars represent the maximum and the minimum values of n and m . Dotted lines describe a pure single-strand cleavage pathway, as described by the Freifelder-Trumbo relationship.³

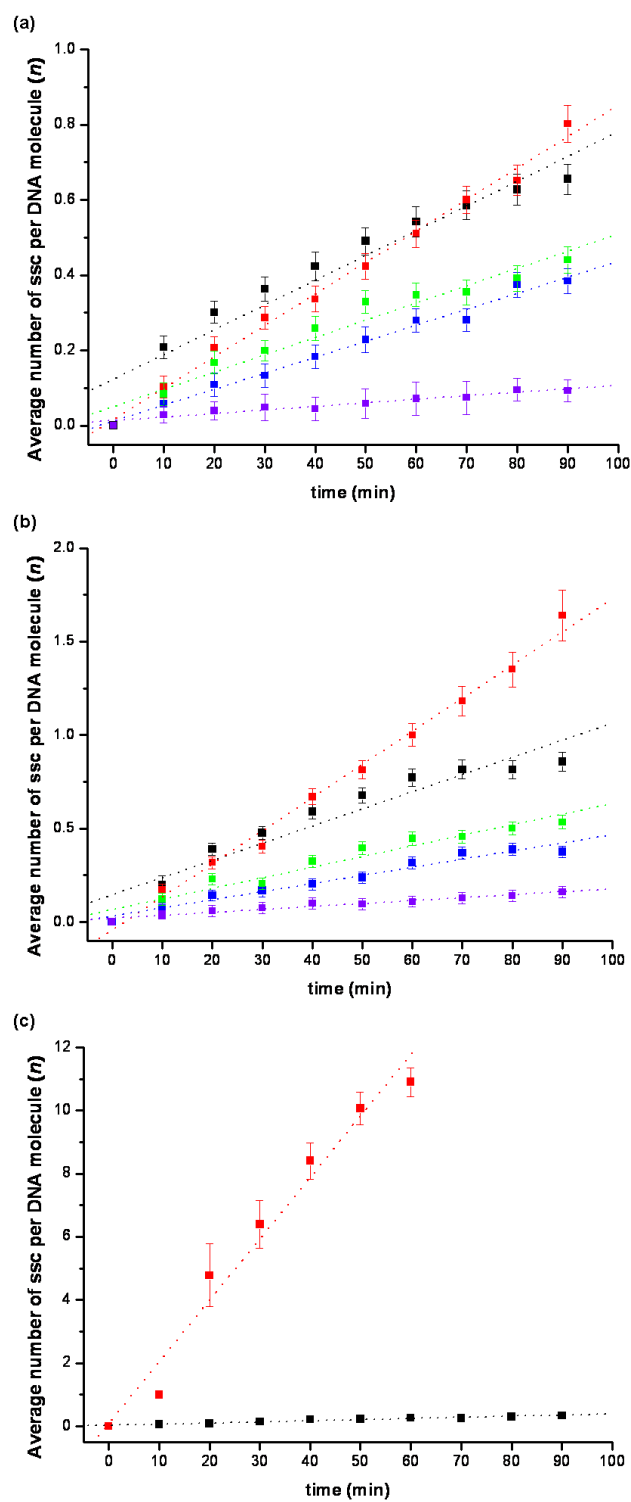


Figure S8: Number of single-strand cuts (n) as a function of time per DNA molecule for (a) Fe(II)-1 (■), Fe(II)-2 (■), Fe(II)-3 (■), Fe(II)-4 (■) and Fe(II)-5 (■) under photo irradiation at 473 nm (30.3 mW); (b) Fe(II)-1 (■), Fe(II)-2 (■), Fe(II)-3 (■), Fe(II)-4 (■) and Fe(II)-5 (■) under photo irradiation at 400 nm (17.4 mW); (c) Fe(II)-2 under ambient lighting (■) and photo irradiation at 355 nm (24.6 mW) (■). Dashed lines represent the linear fit through the data points. Conditions: 1.0 μ M complex, 0.1 μ g/ μ l pUC18 plasmid DNA (150 μ M bp), 10 mM Tris-HCl (pH 8.0), 37 $^{\circ}$ C. Dashed lines represent the linear fit through the data points.

Table S2: Rate constants of DNA cleavage (k_{obs}) in the absence and presence of photo irradiation.

reagents	Cleavage rate (min^{-1}) Ambient lighting	Cleavage rate (min^{-1}) 473 nm (30.3 mW)	Cleavage rate (min^{-1}) 400.8 nm (17.4 mW)	Cleavage rate (min^{-1}) 355 nm (24.6 mW)
Fe^{II} -1	0.0035 ± 0.0003^a ($R^2 = 0.947$)	0.0066 ± 0.0006 ($R^2 = 0.9296$)	0.0092 ± 0.0010 ($R^2 = 0.9154$)	^c
Fe^{II} -2	0.0035 ± 0.0001 ($R^2 = 0.979$)	0.0084 ± 0.0002 ($R^2 = 0.9934$)	0.0177 ± 0.0006 ($R^2 = 0.9922$)	0.196 ± 0.015^d ($R^2 = 0.9721$)
Fe^{II} -3	0.0028 ± 0.0002^a ($R^2 = 0.965$)	0.0043 ± 0.0002 ($R^2 = 0.9871$)	0.0044 ± 0.0003 ($R^2 = 0.9649$)	^c
Fe^{II} -4	^b	0.0046 ± 0.0004 ($R^2 = 0.9539$)	0.0057 ± 0.0005 ($R^2 = 0.9482$)	^c
Fe^{II} -5	^b	0.0009 ± 0.0001 ($R^2 = 0.9397$)	0.0016 ± 0.0001 ($R^2 = 0.9582$)	^c

1 μM iron complex, 0.1 $\mu\text{g } \mu\text{L}^{-1}$ supercoiled pUC18 DNA (150 μM bp), Tris-HCl buffer (pH 8.0), 37 °C. A correction factor of 1.31 is used for the reduced EtBr uptake capacity of supercoiled plasmid pUC18 DNA. ^aThe cleavage rate was obtained within 60 min; ^bThe cleavage rate can not be obtained through the small numbers of single-strand cuts; ^cThe cleavage rate can not be obtained since double-strand cleavage pathway was involved; ^dThe cleavage rate was obtained within 60 min, which is before the DNA cleavage process reaches the limit of accurate quantification.

Fluorescence emission spectra of 3-5 and Fe(II)-3-5

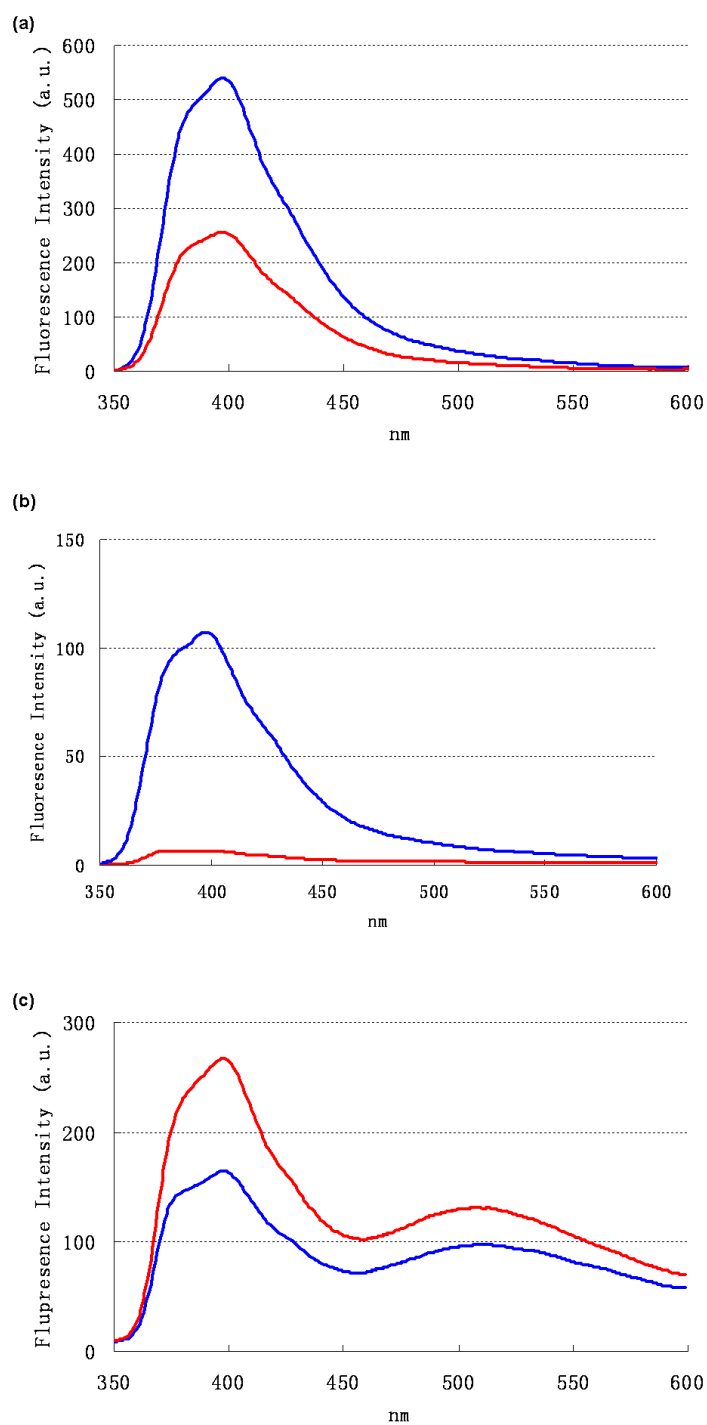


Figure S9: Fluorescence emission spectra in 10 mM Tris-HCl buffer (pH 8.0) at 25 °C for (a) 1 μM **3** (—) and Fe(II)-**3** (—); (b) 8 μM **4** (—) and Fe(II)-**4** (—); (c) 1 μM **5** (—) and Fe(II)-**5** (—).

Mechanistic investigation on Fe(II)-1

Table S3: Numbers of single-strand cuts per DNA molecule (n) with Fe(II)-1 at 30 min with different ROS scavengers.

conditions	n				
	No additive	NaN ₃	DMSO	SOD	SOD + catalase
Ambient lighting	0.285 ± 0.032	0.271 ± 0.032	0.263 ± 0.035	0.175 ± 0.031	0.080 ± 0.030
355 nm (25 mW)	2.09 ± 0.24 (0.056 ± 0.030)*	1.06 ± 0.07 (0.029 ± 0.022)*	1.67 ± 0.14 (0.045 ± 0.028)*	1.05 ± 0.07 (0.035 ± 0.025)*	1.00 ± 0.06
400.8 nm (17 mW)	0.474 ± 0.034	0.355 ± 0.031	0.365 ± 0.032	0.372 ± 0.033	0.130 ± 0.033
473 nm (30 mW)	0.365 ± 0.034	0.306 ± 0.033	0.218 ± 0.031	0.264 ± 0.030	0.118 ± 0.029

* Number of double-strand DNA cleavage per DNA molecule (m).

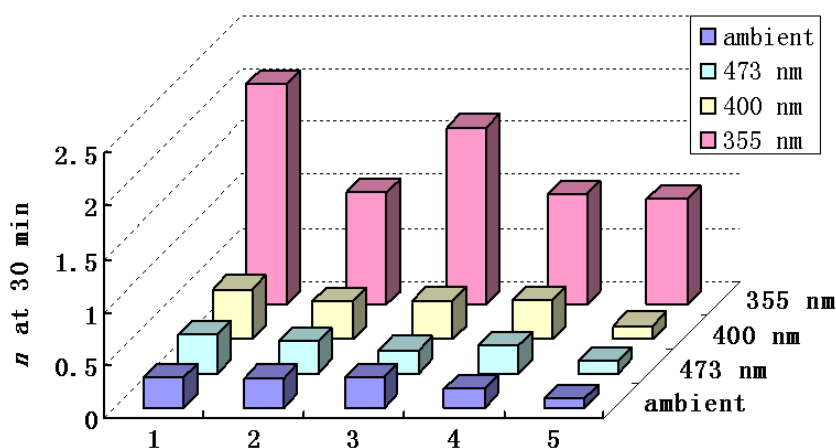


Figure S10: Calculated average numbers of single-strand cuts per DNA molecule (n) of Fe-1 at 30 min with: (1) no ROS scavengers; (2) NaN₃; (3) DMSO; (4) SOD; (5) SOD + catalase. Conditions: 1.0 μM complex, 0.1 μg/μl pUC18 plasmid DNA (150 μM bp), 10 mM Tris-HCl (pH 8.0), 37 °C; ambient lighting, irradiation at 355 nm (pulsed laser, 24.6 mW), 400.8 nm (CW laser, 17.4 mW) and 473 nm (CW laser, 30.3 mW), respectively.

- (1) Montalti, M.; Credi, A.; Prodi, L.; Gandolfi, M. T. *Handbook of Photochemistry*, 3rd ed.; CRC Press: Boca Raton, FL, **2006**.
- (2) van den Berg, T. A.; Feringa, B. L.; Roelfes, G. *Chem. Commun.* **2007**, 180-182.
- (3) Freifelder, D.; Trumbo, B. *Biopolymers* **1969**, 7, 681-693.
- (4) Li, Q.; van den Berg, T. A.; Feringa, B. L.; Roelfes, G. *Dalton Trans.* **2010**, 39, 8012-8021.